

Supplementary Material

**Absence of systemic oxidative stress and increased CSF prostaglandin F<sub>2α</sub> in progressive MS**

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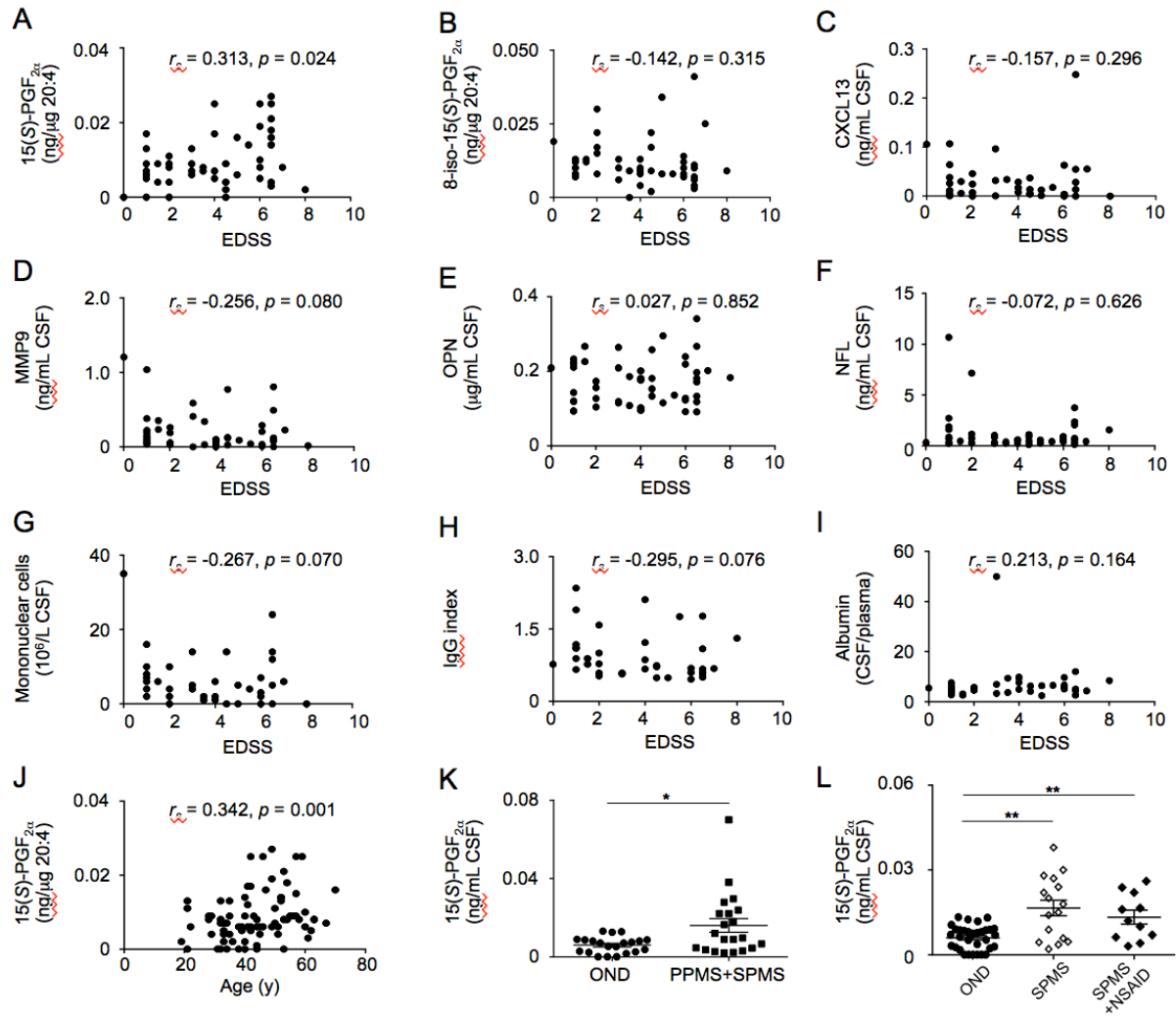
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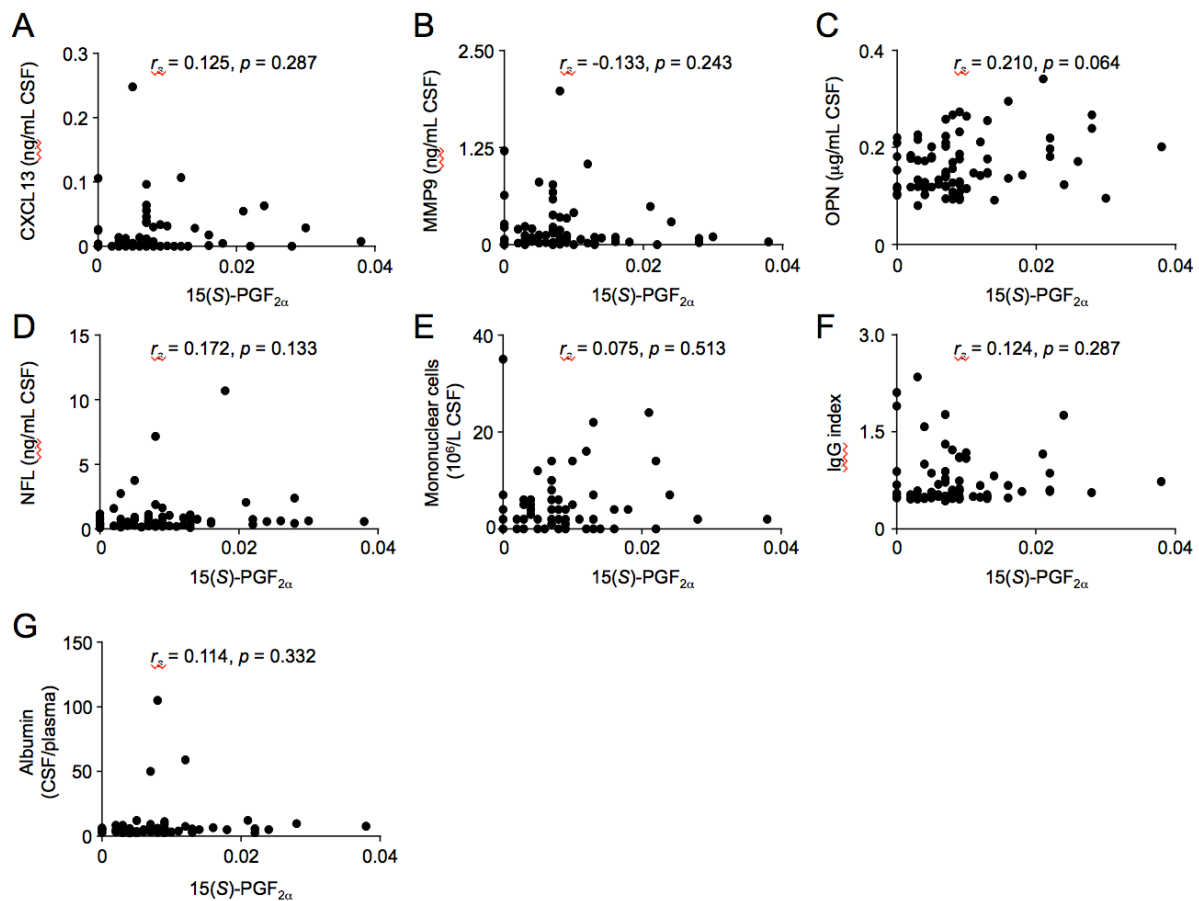
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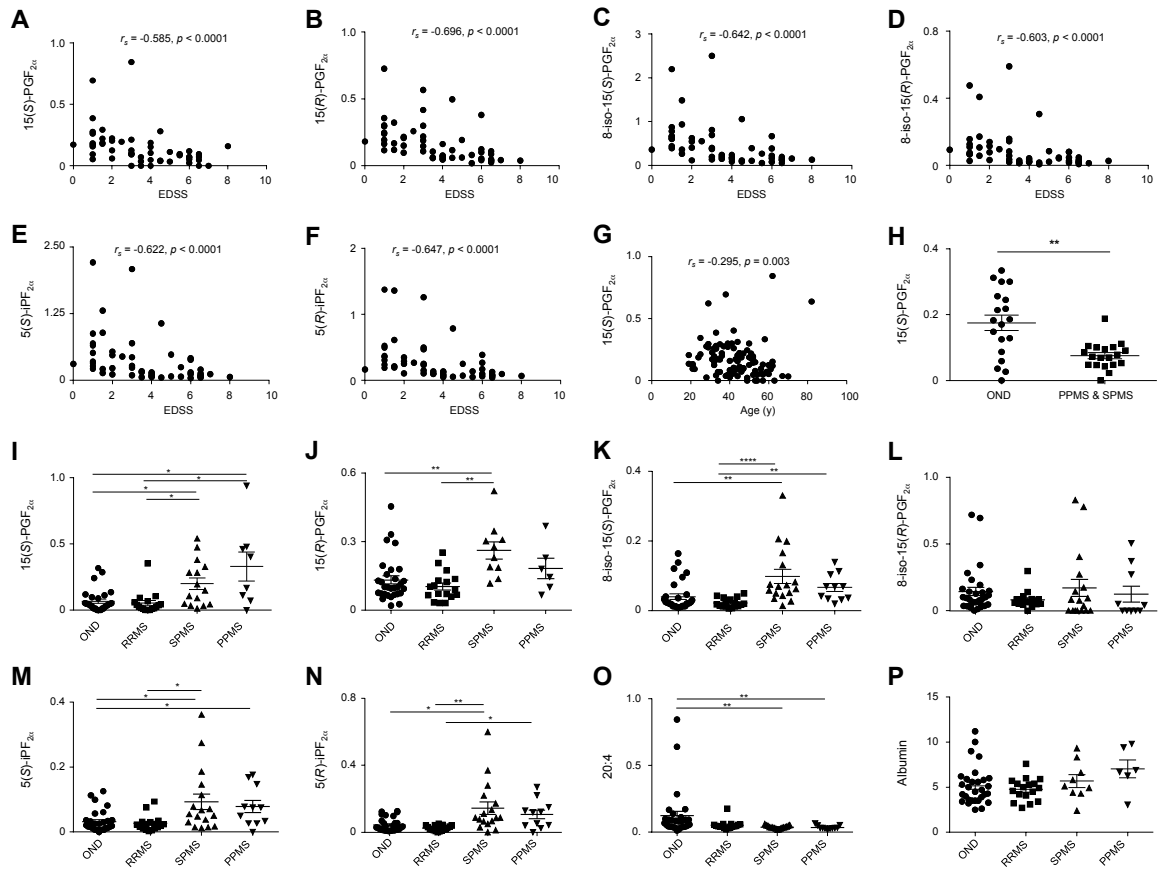
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**Figure e-1.** PGF<sub>2α</sub> but not other CSF biomarkers correlates with MS disease severity. Correlation analyses of disease severity (EDSS) in MS patients with CSF content of (A) 15(S)-PGF<sub>2α</sub>, (B) 8-iso-15(S)-PGF<sub>2α</sub>, (C) Chemokine (C-X-C Motif) Ligand 13 (CXCL13), (D) matrix metalloproteinase 9 (MMP9), (E) osteopontin (OPN), (F) neurofilament light chain protein NFL, (G) mononuclear cell count, (H) IgG index, and (I) albumin CSF/plasma ratio. (J) Correlation analyses of 15(S)-PGF<sub>2α</sub> in CSF with age. (K) Comparison of the content of 15(S)-PGF<sub>2α</sub> in CSF from patients with progressive MS compared with age-matched OND controls. (L) Effect of NSAIDs on the concentration of PGF<sub>2α</sub> in CSF of patients with SPMS compared to OND controls. (A-J) Correlation was determined by Spearman's ranked correlation at 95% confidence interval,  $r_s$ : Spearman's coefficient of correlation. (K-L) Statistical significance was determined by Mann-Whitney. \* $p < 0.05$  and \*\* $p < 0.01$ .



*Figure e-2.* CSF PGF<sub>2α</sub> is not associated with validated biomarkers of MS. Correlation analyses of CSF concentrations of 15(S)-PGF<sub>2α</sub> (ng/mL) and (A) chemokine CXCL13, (B) matrix metalloproteinase 9 (MMP9), (C) osteopontin (OPN), (D) neurofilament light chain protein (NFL), (E) mononuclear cell count, (F) IgG index, and (G) albumin CSF/plasma ratio. Spearman's ranked correlation at 95% confidence interval. Statistical significance was assumed when  $p < 0.05$ .



*Figure e-3.* Plasma F<sub>2</sub>-isoprostanes and PGF<sub>2α</sub> decrease with increasing disease severity independent of age, while the disease-associated increase in CSF PGF<sub>2α</sub> likely originates from increased local enzymatic oxidation of 20:4 rather than circulating PGF<sub>2α</sub>. Correlation analyses of disease severity (EDSS) with plasma concentrations (ng/mL) of (A) 15(S)-PGF<sub>2α</sub>, (B) 15(R)-PGF<sub>2α</sub>, (C) 8-iso-15(S)-PGF<sub>2α</sub>, (D) 8-iso-15(R)-PGF<sub>2α</sub>, (E) 5(S)-iPF<sub>2α</sub> and (F) 5(R)-iPF<sub>2α</sub>. (G) Correlation analyses of the plasma content (ng/mL) of 15(S)-PGF<sub>2α</sub> with age. (H) Comparison of plasma content (ng/mL) of 15(S)-PGF<sub>2α</sub> in MS patients and age-matched OND controls. (I-P) CSF/plasma ratio of 15(S)-PGF<sub>2α</sub>, 15(R)-PGF<sub>2α</sub>, 8-iso-15(S)-PGF<sub>2α</sub>, 8-iso-15(R)-PGF<sub>2α</sub>, 5(S)-iPF<sub>2α</sub>, 5(R)-iPF<sub>2α</sub>, 20:4 and albumin. Data are shown for individuals and as means ± SEM. (A-G) Spearman's ranked correlation at 95% confidence interval. (H-P) Statistical significance determined by the Mann-Whitney test.